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THE RESPONSE OF TISSUE ELECTROLYTES TO RESPIRATORY ACIDOSIS

Carol J. Amick

1959

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THE RESPONSE OF TISSUE ELECTROLYTES
TO RESPIRATORY ACIDOSIS

by

Carol J. Amick
Wellesley College, B.A., 1955

A Thesis Presented to the
Faculty of the Yale University School of Medicine
In Candidacy for the Degree of
Doctor of Medicine

Department of Internal Medicine

1959



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ACKNOWLEDGEMENT

I wish to express my sincere appreciation to Dr. Franklin H. Epstein and Dr. Howard Levitin for their guidance and encouragement in this investigation and to thank Mr. Donald McKay, Mrs. Oleg Myketey, and Mrs. George Taborsky for their technical assistance.

the following words are engraved on the
bottom of the base of the pedestal.
The pedestal is inscribed with the
name of the author and the date.

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INTRODUCTION

Various mechanisms exist by which the body may buffer acidosis and thus prevent a disastrous increase in the hydrogen ion concentration of body fluids. Renal and respiratory regulation and intra and extracellular buffer systems all contribute to the maintenance of homeostasis. In both metabolic and respiratory acidosis renal compensatory responses occur. In acidosis induced by the continued inhalation of carbon dioxide, the organism no longer has the respiratory system available for pH adjustments.

It is well established that in metabolic acidosis sodium and to a lesser extent potassium are removed from bone and muscle and participate in the buffering of mineral acids (1-5). This occurs presumably by an exchange of intracellular cation for extracellular hydrogen ion with a concomitant decrease in ionization of cell phosphate and proteinate. It has not been clearly delineated whether or not this also occurs in respiratory acidosis. On the basis of indirect plasma and red cell studies it has been implied that this is true (6-8). Direct analysis of tissue has not given a clear answer (9).

In order to evaluate the role of tissue cations in respiratory acidosis, analyses of muscle, bone, liver, and plasma were made on normal rats which had been exposed to 8% carbon dioxide for 24 hours. Nephrectomized rats were included

in this experiment in order to evaluate the renal contribution to any observed effect. Rats which had been previously placed on low sodium and low potassium diets were also studied to determine how this would affect the response to respiratory acidosis. Part of this work has been previously reported (10).

METHOD

White Sprague-Dawley rats were maintained on a normal, low sodium, or low potassium diet. The composition of these diets is given in Table I. These animals had been previously trained to take a single 40 minute feeding per day. Following feeding, the animals were placed in an airtight lucite chamber with a controlled inflow of $8 \pm 0.5\%$ carbon dioxide in air for 24 hours. The oxygen content remained $19 \pm 1\%$ throughout. Water was allowed ad libitum during the study period except for the nephrectomized rats. No food was allowed during the time in the chamber. At the end of the experimental period the animals were removed from the chamber, anesthetized lightly with pentobarbital and sacrificed in room air. As indicated in several of the experiments, after being anesthetized, the head of the animal was placed in a relatively airtight hood with a rubber cuff around the neck. Eight per cent carbon dioxide in air continuously flowed through the hood preceding and during the sacrifice.

A vertical mid-abdominal incision was made and the animal was exsanguinated via the abdominal aorta using a heparinized syringe containing mineral oil. The procedure was terminated when the blood ceased flowing smoothly. The entire liver was removed and placed without blotting into a dry previously weighed ground glass stoppered weighing bottle. Beyond handling the tissue as expeditiously as possible, no attempt was

the most prominent among the other towns around it.
The town is built on a hill, and has a very fine view over the surrounding country. It is situated on the river *Arno*, which flows through the town, and is crossed by several bridges. The town is surrounded by a wall, and has a number of towers and fortifications. The people of the town are mostly engaged in agriculture and trade. They are a hardy and enterprising race, and are well known for their skill in building and engineering. The town is also famous for its wine, which is highly esteemed throughout Italy. The people of the town are very hospitable, and are always ready to welcome strangers. The town is a popular resort for tourists, who come to enjoy the beauty of the surrounding country, and the pleasure of a quiet holiday. The town is also a centre for the trade of wool and silk, and is well known for its fine fabrics. The town is a centre for the trade of wool and silk, and is well known for its fine fabrics. The town is a centre for the trade of wool and silk, and is well known for its fine fabrics.

made to prevent water loss during transfer. Long skin incisions were made on the hind legs. The quadriceps muscles were removed with particular care to exclude fat, fascia and tendonous insertions. The muscles from both extremities were placed together in one covered weighing bottle. The femurs were carefully scraped clean of attached muscle and tendon. The heads and distal epiphyses were cut off. The marrow was removed by repeated insertions of a #17 needle through the medullary canal. The marrow-free shafts were then placed together in a single weighing bottle.

The wet specimens were dried for 5 days in an oven at 97-103°C.. The tissue was ground to a fine powder in individual mortars and redried for an additional 24 hours. The total weight lost during the two dryings was assumed to be the water content of the tissue. After the second drying the neutral fat was removed by extracting three times with about 30 cc. anhydrous diethyl ether. The bone was not fat extracted. The extraction was done in the weighing bottle with the cover tightly in place to minimize the absorption of water from the atmosphere. It had been observed earlier that electrolytes were lost during this procedure if the ether contained water. After 6 to 8 hours the clear supernatant was carefully siphoned from the specimen with a capillary tube attached to a vacuum. The tip of the tube was covered with a small piece of filter paper which prevented agitation during the procedure. After the third extraction the tissue was dried first in room air and then for 24 hours in the oven. The loss of weight in this

and the other two were in the same condition. The first was a small
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small yellowish-green bird with a black cap and a white patch on each side of
the neck. It had a short crest and a long tail.

procedure determined the amount of neutral fat in the specimen. Following extraction, the fat-free dry specimen was re-ground to a fine homogenous powder.

Electrolyte Determinations (11). Specimens of powdered, fat-free liver and muscle, weighing 500 mgm., were placed individually in small Erlenmeyer flasks to which were added 2.00 cc. of 0.0500 N silver nitrate and 8 cc. of concentrated nitric acid. The specimens were digested overnight on a steam table. The temperature of the digestion mixture ranged from about 75° to 90°C. After digestion the solution was transferred quantitatively to a 25 cc. volumetric flask through clean glass wool. The resulting diluted sample was used for electrolyte determinations. The chloride concentration was determined by the Volhard method (11). 5.00 cc. aliquots were placed in duplicate chloride tubes to which were added 3 cc. concentrated nitric acid and saturated potassium permanganate solution. The tubes were heated in a water bath until clear and then cooled with ice water. Ferric alum indicator was added and the solutions titrated with 0.02 N sodium thiocyanate. A correction factor was determined. The sodium and potassium concentrations were determined in duplicate on diluted aliquots by indirect flame photometry with the Baird spectrophotometer.

Specimens of bone weighing 250 mgm. were digested overnight in Erlenmeyer flasks to which had been added 1.00 cc. of 0.0500 N silver nitrate and 4 cc. of concentrated nitric acid. The digest was transferred quantitatively to a volumetric flask through clean glass wool. Sodium, potassium, and chlor-

ide were determined in duplicate as indicated above. Phosphorus was determined by a modification of the method of Fiske and Subbarow (12). To a 12.5 cc. volumetric flask were added 0.500 cc. of diluted specimen, 2 cc. water, and 4 cc. of 20% trichloroacetic acid. 4.00 cc. of this solution, 2.00 cc. of 0.5 N sulfuric acid, 0.200 cc. of 2.5% molybdate and 0.100 cc. of sulfonic acid reagent were added to a calibrated cuvette. After 30 minutes the sample and standard solutions were read at 700 m μ wavelength in a Coleman Jr. spectrophotometer.

Plasma sodium and potassium were determined by indirect flame photometry with a Baird spectrophotometer, and the carbon dioxide content by the method of Van Slyke and Neill (13). Plasma chloride was determined either by Volhard titration (11) or by potentiometric titration with silver nitrate as indicated. The air in the chamber was analyzed periodically for carbon dioxide and oxygen in a Scholander gas analysis apparatus (14).

Group I Normal Diet Twenty female rats were placed on the normal diet with trained feeding for 2 weeks prior to the experiment. Weight at sacrifice was 188 to 229 grams. There were 10 control and 10 experimental animals. The control animals were those which remained in room air throughout the 24 hour period and the experimental animals were those which were exposed to 8% carbon dioxide.

Group Ib Eight experimental male rats on a normal diet with trained feeding for three weeks were sacrificed while in the carbon dioxide hood. Sacrifice weight was 282 to 502 grams.

Group II Nephrectomy Thirteen male rats, weighing 312 to

and the other hand, as the time of maturation approaches, the seeds become more and more difficult to germinate, and finally the seeds are no longer able to germinate at all. This is called seed dormancy. In some cases, however, the seeds remain dormant for a long time, and then germinate readily. This is called after-ripening. In other cases, the seeds remain dormant for a long time, and then germinate readily. This is called after-ripening. In other cases, the seeds remain dormant for a long time, and then germinate readily. This is called after-ripening.

After-ripening is a common phenomenon in many plants, and it is particularly well known in cereals. In wheat, for example, the seeds are harvested when they are still green and immature, and are then stored in a dry place. After a period of time, usually about two weeks, the seeds begin to germinate, and this process continues until the seeds are fully ripe. This is called after-ripening. In other cases, the seeds remain dormant for a long time, and then germinate readily. This is called after-ripening.

396 grams at sacrifice, which had been on an untrained Purina Chow diet were included in this group. The animals were placed under ether anesthesia and a vertical mid-abdominal incision was made. The renal pedicles were tied off with single silk ligatures bilaterally and the two kidneys were removed with a minimum of manipulation. The adrenal glands remained in place and the incision was closed with metal clips. Following nephrectomy they did not receive food or water prior to sacrifice. The animals recovered from the surgery for one hour and then 6 of them were placed in the carbon dioxide chamber for 24 hours. The remainder served as controls. Three of the experimental animals were exsanguinated while in the carbon dioxide hood. There were no significant differences in the plasma electrolyte determinations of these animals as compared to the 3 killed in room air and they were considered as a unit.

Group III Low Sodium Diet Eight male rats, weighing 29 $\frac{1}{4}$ to 37 $\frac{1}{4}$ grams at sacrifice, were placed on the low sodium diet with trained feeding for three weeks prior to the experiment. There were 4 control and 4 experimental animals.

Group IV Low Potassium Diet Ten male rats, weighing 260 to 312 grams at sacrifice, were placed on the low potassium diet with trained feeding for three weeks prior to the experiment. There were 6 control and 4 experimental animals. The experimental rats were sacrificed in the carbon dioxide hood.

CALCULATIONS

The intracellular sodium and potassium of fat-free muscle were calculated according to the method of Hastings and Eichelberger (15). These calculations are based on the assumptions that chloride is entirely extracellular and that sodium, potassium and chloride are present in the extracellular fluid as a result of the Gibbs-Donnan effect. The details of these calculations are indicated below.

- (1) Gm. H₂O per kg. muscle - determined experimentally as the sum of the water lost in the first and second dryings.
- (2) Gm. fat per kg. muscle = %fat in dry muscle (determined experimentally) x weight of dry muscle per kg. wet muscle.
- (3) Gm. FFWM¹ per kg. muscle = 1000 minus (2).
- (4) Gm. H₂O per kg. FFWM = 1000 x (1) ÷ (3).
- (5) Gm. FFS² per kg. FFWM = 1000 minus (4).
- (6) Cl_t³, Na_t, and K_t = Cl, Na, and K per gm. FFS (determined experimentally) x (5).
- (7) Cl_{ECF}⁴ = [Cl]_p⁵ ÷ (0.93⁶ x 0.95⁷).

¹ Fat-free wet muscle.

² Fat-free solid.

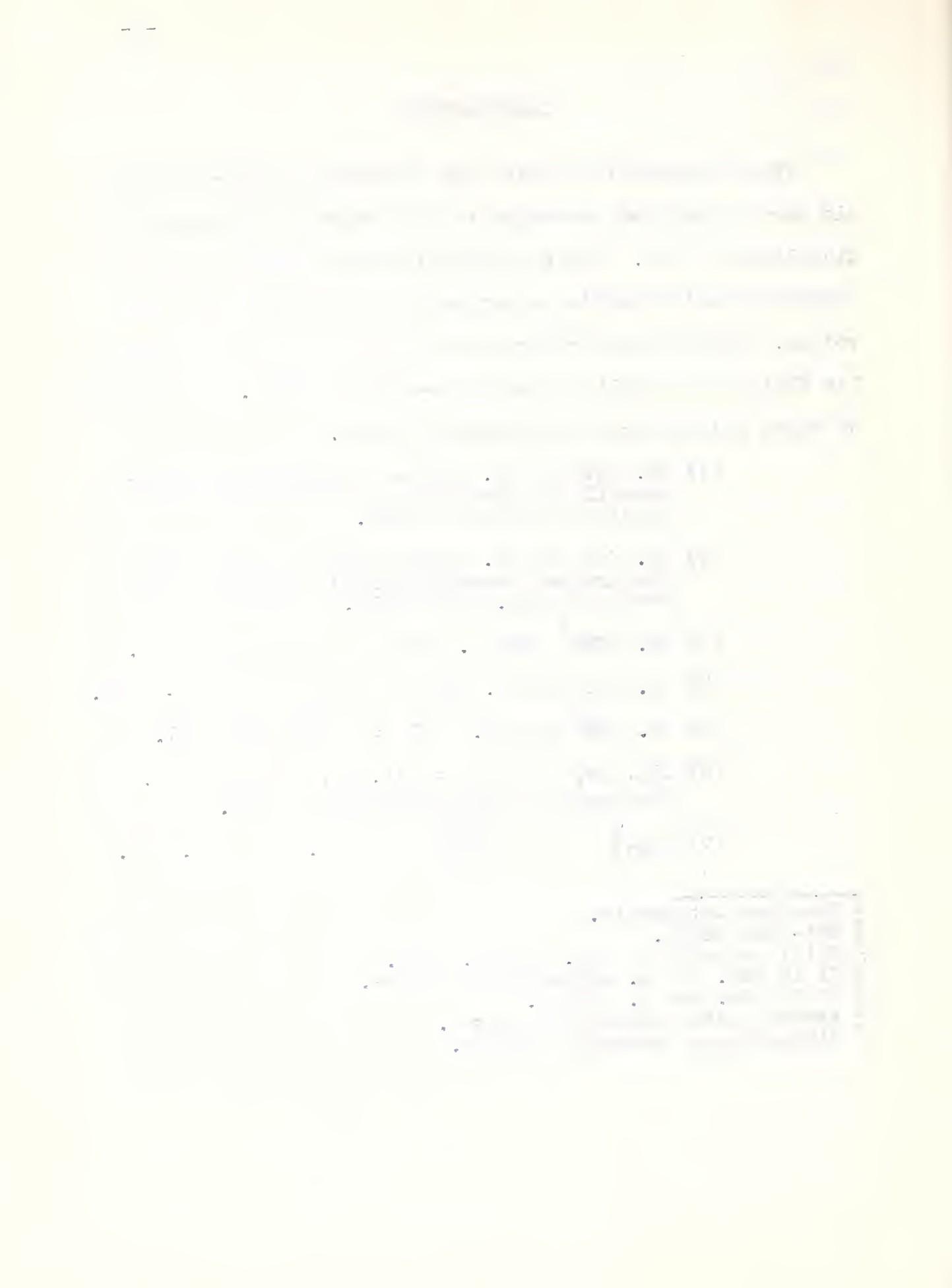
³ Total chloride in mEq. per kg. FFWM.

⁴ Cl in mEq. per L. extracellular phase.

⁵ Cl in mEq. per L. plasma.

⁶ Assumed water content of plasma.

⁷ Gibbs-Donnan correction factor.



$$(8) \text{ ECW}^8 = [(Cl_t \times 1000) \div Cl_{ECF}] \times 0.99^9.$$

$$(9) \text{ ICW}^{10} = H_2O^{11} \text{ minus ECW.}$$

$$(10) \text{ Na}_e^{12} = [([Na]_p \times 0.95) \div 0.93] \times \text{ECW.}$$

$$K_e = [([K]_p \times 0.95) \div 0.93] \times \text{ECW.}$$

$$(11) \text{ Na}_i^{13} = \text{Na}_t \text{ minus } \text{Na}_e.$$

$$K_i = K_t \text{ minus } K_e.$$

$$(12) \text{ MEq. Na per kg. intracellular } H_2O = \\ (\text{Na}_i \times 1000) \div \text{ICW.}$$

$$\text{MEq. K per kg. intracellular } H_2O = \\ (K_i \times 1000) \div \text{ICW.}$$

DISCUSSION OF CALCULATIONS

The question whether or not chloride may be considered entirely extracellular has been thoroughly reviewed by Manery (16). Her general conclusion is that in the particular case of muscle this is justified. A possible exception to this is when there is an elevated serum potassium. It should be noted that in three nephrectomized rats the calculated intracellular sodium content was negative. This result could be due to 1) in-

⁸ Extracellular H_2O per kg. FFWM.

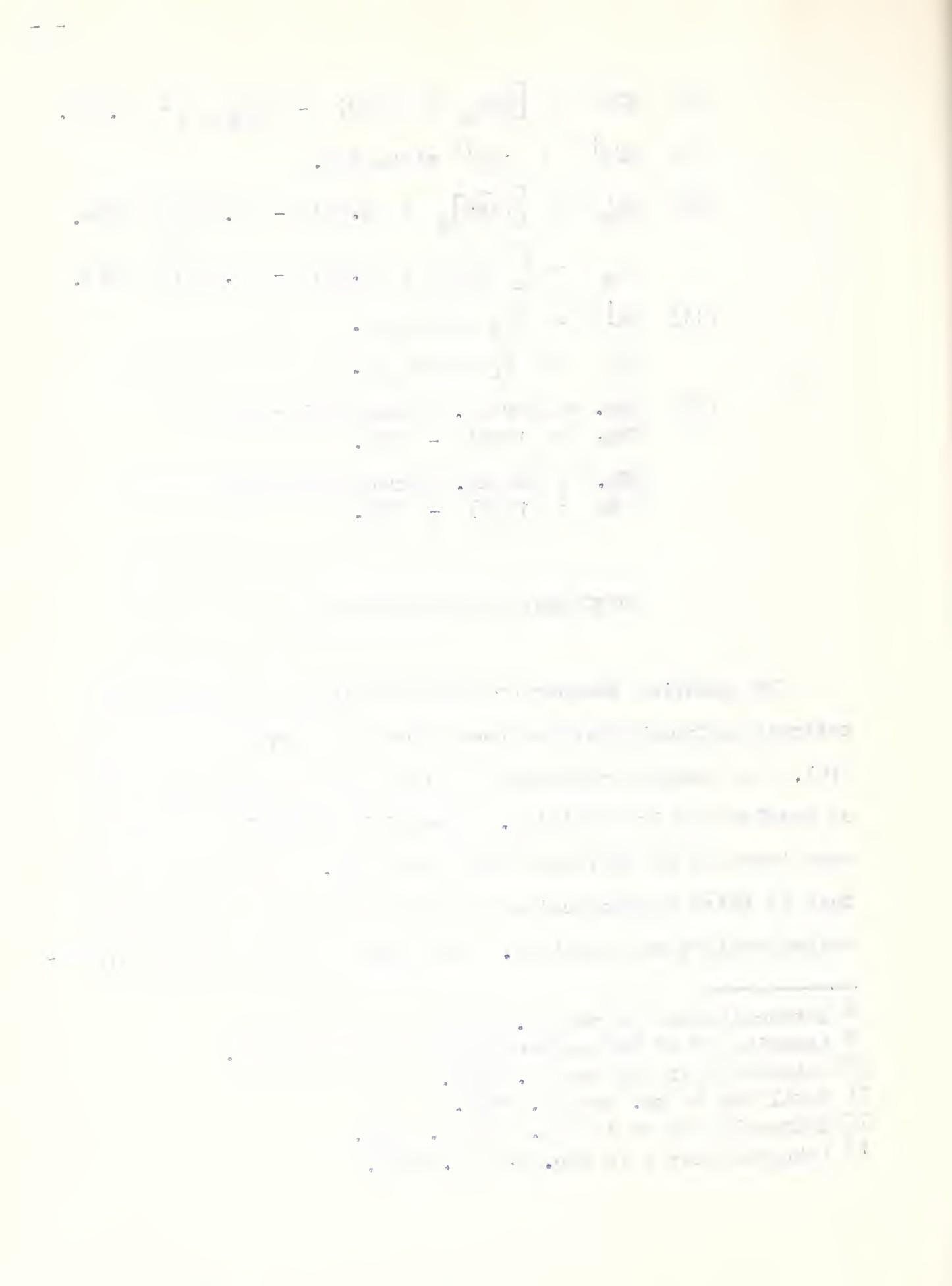
⁹ Assuming 1% of the extracellular phase is solid.

¹⁰ Intracellular H_2O per kg. FFWM.

¹¹ Total H_2O in gm. per kg. FFWM.

¹² Extracellular Na in mEq. per kg. FFWM.

¹³ Intracellular K in mEq. per kg. FFWM.



creased presence of tendon or connective tissue in the muscle specimens where chloride may be present in greater concentration than as a plasma ultrafiltrate (16), 2) errors in the analyses or 3) intracellular chloride. The first two were probably not the cause since similar dissection methods were used in all cases and the standard deviation was no greater than in the other experiments. It is possible that, in the presence of an elevated serum potassium, chloride moved intracellularly. In vitro, frog muscle has been found to gain chloride in the presence of elevated extracellular potassium (17).

The intracellular concentrations of potassium and sodium in the liver were not calculated for several reasons. More chloride is present in the liver than can be accounted for on the basis of extracellular water. The glycogen content may vary considerably and it is known that the concentration of potassium in bile is higher than that in plasma (18).

COMPARISON OF THIGH AND ABDOMINAL MUSCLE

In comparing the published data on the electrolyte composition of muscle it is important to realize that variation occurs not only with age but according to the location of the muscle analyzed. Holliday et al. found significant difference in the potassium content of fat-free dry muscle from back and thigh, but reported that the calculated concentration of potassium per kilogram intracellular water did not differ significantly (19).

The abdominal muscles of the rats on the low sodium diet (Group III) were carefully dissected free of fascia and fat and analyzed as previously indicated. The sodium, potassium and chloride content of the thigh and abdominal muscles of the same animals are given in Table II. There were significant differences in the electrolyte content of the fat-free dry muscle between the two groups. However, when expressed as mEq. of sodium or potassium per kilogram of intracellular water, differences between the muscle from the thigh and abdomen disappeared or decreased markedly, as found by Holliday.

One cannot make the assumption, however, that the intracellular sodium and potassium are the same throughout the muscle of the body. In both Holliday's data and those reported here there was a marked increase in the standard deviation of the calculated values over the analyzed values which might mask real differences.

It was reassuring to note that any shift in the electrolyte concentrations of the control animals and those exposed to carbon dioxide was in the same direction in both the abdominal and thigh muscles.

EXSANGUINATION IN CARBON DIOXIDE

In the initial experiments all the rats including those exposed to carbon dioxide were sacrificed in room air. During this two to five minute period the experimental animals were able to blow off carbon dioxide with a concomitant elevation of plasma pH. In order to avoid this, in the subsequent studies the experimental animals were sacrificed in the carbon dioxide hood previously described. In the experimental nephrectomized rats half were exsanguinated in room air and the remainder in carbon dioxide. No significant difference was noted between these animals in any of the studies.

Rats on a normal diet exposed to carbon dioxide for 24 hours were sacrificed by the two methods and are compared in Table III. Statistically significant differences were present in the sodium content of muscle and in the plasma carbon dioxide content. This latter difference may be considered to be due to the higher plasma pCO_2 of the animals sacrificed while still exposed to carbon dioxide. It is apparent that there were no differences in the plasma chloride, sodium or potassium between the two groups. It is probably unjustified to compare these two groups since they differed in both weight and sex and variations in electrolyte concentration on that basis might mask significant differences.

It might have been predicted that there would be no change in plasma electrolytes during the first few minutes of recovery

from chronic respiratory acidosis for it has been noted that although the pH rapidly changes other adjustments occur more slowly (6, 20). Also the data presented here on the nephrectomized animals did not reveal any differences in the electrolyte concentrations between the experimental and control groups.

RESULTS

Plasma The effect of respiratory acidosis on the plasma of normal rats, nephrectomized rats and rats maintained on low sodium and low potassium diets is given in Table IV.

Rats on the regular diet exposed to 8% carbon dioxide for 24 hours had a decrease in plasma chloride of 6.4 mEq. per liter and an increase in plasma carbon dioxide content of 6.3 mEq. per liter over the control animals. In the experimental animals there was a 0.5 mEq. per liter increase in the plasma potassium and no significant change in the plasma sodium concentration.

There were no differences in the plasma electrolyte concentrations of the experimental nephrectomized animals from their controls. In work not reported here, rats which had had mock nephrectomies responded to respiratory acidosis in the same manner as normal rats which had not had surgery.

The experimental rats on the low sodium diet had an 8.7 mEq. per liter decrease in the plasma chloride and a 6.3 mEq. per liter increase in the plasma carbon dioxide content from their control animals. There were no significant changes in the plasma sodium or potassium.

The control rats on the low potassium diet had the plasma electrolyte changes of potassium depletion. Compared with the control rats on the normal diet they had a decrease in the plasma potassium and chloride and an increase in the plasma carbon

dioxide content. On exposure to 8% carbon dioxide the potassium depleted animals had a 6.5 mEq. per liter decrease in plasma chloride and a 9.3 mEq. per liter rise in carbon dioxide content over their controls. There was an elevation in the plasma potassium of 0.6 mEq. per liter and no significant change in the plasma sodium.

In summary, the effect of 8% carbon dioxide inhalation on rats on normal, low sodium and low potassium diets was to decrease the plasma chloride concentration by about 6 mEq. per liter and to increase the plasma carbon dioxide content by about the same amount. There was either a slight increase in the plasma potassium or no change. There was no change in the plasma sodium concentration. Exposure of nephrectomized rats to 8% carbon dioxide did not change the concentrations of the plasma electrolytes which were studied.

Muscle The effect of respiratory acidosis on the muscle of normal rats, nephrectomized rats and rats maintained on low sodium and low potassium diets is given in Tables V and VI.

In the normal animals exposed to 8% carbon dioxide there was a drop of 1.5 mEq. of potassium per 100 gm. FFDM. This decrease was not reflected in a significant decrease in the potassium concentration of cell water. There were no changes in the sodium, potassium, chloride or water concentrations.

There were no significant changes of muscle electrolytes or water in the nephrectomized rats upon exposure to 8% carbon dioxide.

the first time in the history of the world
that the people of the United States
have been compelled to go to war
with their own Government.

The cause of the rebellion is the same
as that which has always been the cause
of all revolutions - the desire of the
people to be free from the control of
any other power than their own. The
people of the South have always
been free, and they have always
been willing to remain free. They
have always been willing to pay
for their freedom, and they have
always been willing to defend
their freedom.

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always been willing to defend
their freedom.

The experimental rats on the low sodium diet had a significant decrease of 2.7 mEq. potassium per 100 gm. of FFDM and of 8.8 mEq. potassium per kg. of cell water after exposure to carbon dioxide. There was an increase of 3.6 mEq. sodium per kg. of FFWM and an increase of 6.7 mEq. sodium per kg. cell water upon exposure to elevated carbon dioxide. There was no change in the water or chloride content.

The control animals on the low potassium diet had a significant decrease of 9.6 mEq. potassium per 100 gm. FFDM and an increase of 3.3 mEq. sodium per 100 gm. FFDM from the control animals on a normal diet and can thus be considered potassium depleted. Except for the increase of 8.4 mEq. potassium per kg. cell water there were no significant differences in the water or electrolyte concentrations between the experimental and control animals.

Liver The effect of respiratory acidosis on the liver of normal rats, nephrectomized rats and rats maintained on a low sodium diet is given in Table VII.

There were no significant changes of either water or electrolyte concentrations in the normal rats upon exposure to carbon dioxide. There was a significant increase of 1.5 mEq. of potassium per 100 gm. FFDL in the nephrectomized rats in respiratory acidosis over their controls without other changes.

The experimental rats on the low sodium diet had a significantly higher percent water and lower percent fat than their controls. The chloride concentration was 1.7 mEq. per 100 gm.

FFDL lower in the experimental animals. There were no differences in the sodium and potassium concentrations.

Bone The effect of respiratory acidosis on the bone of normal rats, nephrectomized rats and rats maintained on low sodium and low potassium diets is given in Table VIII.

The normal experimental rats had an increase of 0.6 mEq. potassium per 100 gm. dry bone and a decrease of 3.5 mgm. phosphorus per gm. of dry bone without other significant changes.

There were no significant differences in the bone analyses of the experimental and control nephrectomized animals.

The experimental animals on the low sodium and low potassium diets respectively had a decrease of 0.9 and 0.8 mEq. chloride per 100 gm. dry bone, compared to their controls. There were no other significant differences in either group.

the same time, the number of people who have been
killed or injured in the conflict has risen sharply.
The UN estimates that over 100,000 people have
been killed since the conflict began in 2011.
The conflict has also led to a significant increase
in the number of refugees and internally displaced
people. According to the UN, there are currently
over 4 million refugees and IDPs in the region.
The conflict has also had a major impact on the
economy. The economy has suffered from
reduced investment, decreased exports,
and increased inflation. The conflict has
also led to a significant increase in the
cost of living, particularly for those in
poorer areas.

DISCUSSION

In animals with intact kidneys, the most striking effect of respiratory acidosis on the plasma was a consistent increase in the plasma carbon dioxide content and a decrease in the plasma chloride concentration. The increased carbon dioxide content has been shown to be related to increased renal tubular absorption of bicarbonate in the presence of increased pCO_2 (21-23). In acute respiratory acidosis the hypochloremia has been attributed in part to a chloride shift into the red blood cells (8). However, in chronic respiratory acidosis in man, the red blood cell chloride is normal in the presence of hypochloremia (24). Recently it has been shown that rats in respiratory acidosis have a chloruresis of sufficient degree to account for the observed hypochloremia (25). The changes in both carbon dioxide and chloride of plasma, then, are probably chiefly the result of renal action.

In normal rats and in potassium depleted rats a small but significant increase in the plasma potassium occurred in response to respiratory acidosis. Other investigators have shown respiratory acidosis to result in hyperkalemia in dogs which were either nephrectomized or had ligated ureters. Scribner and Burnell (6) exposed dogs with ligated ureters to 30% carbon dioxide and noted a gradual rise of plasma potassium from 4.2 to 7.5 mEq. per liter over four hours. Similar results were obtained in dogs with intact ureters (26). Other

work with nephrectomized dogs in respiratory acidosis showed an increase in the plasma potassium for the first hour but with the continuance of acidosis this returned toward normal (8). Hyperkalemia significantly greater than that of the control animals was not observed in the nephrectomized rats of the present experiments. Part of this discrepancy may be related to species difference and to the marked differences in experimental conditions existing between the present study and those of other workers. It should be noted, however, that the mean plasma potassium was higher in the rats exposed to carbon dioxide than in those breathing room air. A physiological difference might be masked in this case by the small number of experimental animals and a large standard deviation.

Potassium depleted animals demonstrated the expected increase in plasma carbon dioxide content over rats eating a normal diet. Upon exposure to carbon dioxide there was a further increase in the carbon dioxide content of plasma. This is consistent with the work of Roberts, Randall, Sanders and Hood (27) who showed that hypokalemia increased the reabsorption of bicarbonate, but that hyperkalemia reduced to normal the enhanced reabsorption of bicarbonate caused by respiratory acidosis. They proposed that bicarbonate reabsorption varied inversely with the pH of the renal tubular cells, suggesting that increased carbon dioxide and decreased plasma potassium both caused a decrease in cell pH while an elevated plasma potassium would tend to elevate the decreased cellular pH caused by respiratory acidosis. In the potassium depleted

the first time in the history of the country, 1770, when
the British Parliament passed the Stamp Act, which imposed a
tax on all printed paper used for documents, legal and
otherwise. This stamp tax imposed a
heavy burden on the people using stamped paper
for the day-to-day business of America and
was one of the causes of the American Revolution.
The British government, which controlled
the colonies, believed they had the right to collect taxes
from the colonists without their consent.
This was the beginning of the American Revolu-
tion, which began over taxation.
After the revolution, America became an
independent nation, and the new nation
had to establish its own currency and coinage.
The first coinage of the United States was
the silver dollar, which was minted in 1792.
The dollar was divided into 100 cents,
and each cent was divided into 10 mills.
The dollar was also divided into 20 dimes,
and each dime was divided into 10 cents.
The dollar was also divided into 4 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 8 halves,
and each half was divided into 50 cents.
The dollar was also divided into 16 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 32 halves,
and each half was divided into 50 cents.
The dollar was also divided into 64 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 128 halves,
and each half was divided into 50 cents.
The dollar was also divided into 256 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 512 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1024 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2048 halves,
and each half was divided into 50 cents.
The dollar was also divided into 4096 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 8192 halves,
and each half was divided into 50 cents.
The dollar was also divided into 16384 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 32768 halves,
and each half was divided into 50 cents.
The dollar was also divided into 65536 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 131072 halves,
and each half was divided into 50 cents.
The dollar was also divided into 262144 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 524288 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1048576 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2097152 halves,
and each half was divided into 50 cents.
The dollar was also divided into 4194304 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 8388608 halves,
and each half was divided into 50 cents.
The dollar was also divided into 16777216 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 33554432 halves,
and each half was divided into 50 cents.
The dollar was also divided into 67108864 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 134217728 halves,
and each half was divided into 50 cents.
The dollar was also divided into 268435456 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 536870912 halves,
and each half was divided into 50 cents.
The dollar was also divided into 107374184 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 214748368 halves,
and each half was divided into 50 cents.
The dollar was also divided into 429496736 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 858993472 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1717986944 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 3435973888 halves,
and each half was divided into 50 cents.
The dollar was also divided into 6871947776 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 13743895552 halves,
and each half was divided into 50 cents.
The dollar was also divided into 27487791104 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 54975582208 halves,
and each half was divided into 50 cents.
The dollar was also divided into 109951164416 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 219902328832 halves,
and each half was divided into 50 cents.
The dollar was also divided into 439804657664 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 879609315328 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1759218630656 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 3518437261312 halves,
and each half was divided into 50 cents.
The dollar was also divided into 7036874522624 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 14073749045248 halves,
and each half was divided into 50 cents.
The dollar was also divided into 28147498090496 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 56294996180992 halves,
and each half was divided into 50 cents.
The dollar was also divided into 112589992361984 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 225179984723968 halves,
and each half was divided into 50 cents.
The dollar was also divided into 450359969447936 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 900719938895872 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1801439877791744 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 3602879755583488 halves,
and each half was divided into 50 cents.
The dollar was also divided into 7205759511166976 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 14411519022333952 halves,
and each half was divided into 50 cents.
The dollar was also divided into 28823038044667904 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 57646076089335808 halves,
and each half was divided into 50 cents.
The dollar was also divided into 115292152178671616 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 230584304357343232 halves,
and each half was divided into 50 cents.
The dollar was also divided into 461168608714686464 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 922337217429372928 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1844674434858745856 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 3689348869717491712 halves,
and each half was divided into 50 cents.
The dollar was also divided into 7378697739434983424 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1475739547886996688 halves,
and each half was divided into 50 cents.
The dollar was also divided into 2951479095773993376 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 5902958191547986752 halves,
and each half was divided into 50 cents.
The dollar was also divided into 11805916383095973504 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 23611832766191947008 halves,
and each half was divided into 50 cents.
The dollar was also divided into 47223665532383894016 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 94447331064767788032 halves,
and each half was divided into 50 cents.
The dollar was also divided into 188894662129535576064 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 377789324258571152128 halves,
and each half was divided into 50 cents.
The dollar was also divided into 755578648517142304256 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1511157297034284608512 halves,
and each half was divided into 50 cents.
The dollar was also divided into 3022314594068569217024 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 6044629188137138434048 halves,
and each half was divided into 50 cents.
The dollar was also divided into 12089258376274276868096 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 24178516752548553736192 halves,
and each half was divided into 50 cents.
The dollar was also divided into 48357033505097107472384 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 96714067010194214944768 halves,
and each half was divided into 50 cents.
The dollar was also divided into 193428134020388429889536 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 386856268040776859779072 halves,
and each half was divided into 50 cents.
The dollar was also divided into 773712536081553719558144 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 154742507216310743911628 halves,
and each half was divided into 50 cents.
The dollar was also divided into 309485014432621487823256 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 618970028865242975646512 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1237940057730485951293024 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2475880115460971902586048 halves,
and each half was divided into 50 cents.
The dollar was also divided into 4951760230921943805172096 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 9903520461843887610344192 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1980704092368777522068838 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 3961408184737555044137676 halves,
and each half was divided into 50 cents.
The dollar was also divided into 7922816369475110088275352 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1584563273895022017655070 halves,
and each half was divided into 50 cents.
The dollar was also divided into 3169126547785044035310140 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 6338253095570088070620280 halves,
and each half was divided into 50 cents.
The dollar was also divided into 12676506191140176141240560 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 25353012382280352282481120 halves,
and each half was divided into 50 cents.
The dollar was also divided into 50706024764560704564962240 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 10141204952912140912932480 halves,
and each half was divided into 50 cents.
The dollar was also divided into 20282409855824281825864960 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 40564819711648563651729920 halves,
and each half was divided into 50 cents.
The dollar was also divided into 81129639423297127303459840 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 162259278846594254606919680 halves,
and each half was divided into 50 cents.
The dollar was also divided into 324518557693188509213839360 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 649037115386377018427678720 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1298074230772754036855357440 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2596148461545508073710714880 halves,
and each half was divided into 50 cents.
The dollar was also divided into 5192296923091016147421429760 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 10384593846182332294842859520 halves,
and each half was divided into 50 cents.
The dollar was also divided into 20769187692364664589685719040 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 41538375384729329179371438080 halves,
and each half was divided into 50 cents.
The dollar was also divided into 83076750769458658358742876160 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 166153501538917316717457532320 halves,
and each half was divided into 50 cents.
The dollar was also divided into 332307003077834633434915064640 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 664614006155669266869830129280 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1329228012311338533739660358560 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2658456024622677067479320717120 halves,
and each half was divided into 50 cents.
The dollar was also divided into 5316912049245354134958641434240 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1063382409849078826991728286840 halves,
and each half was divided into 50 cents.
The dollar was also divided into 2126764819698157653983456573680 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 4253529639396315307966913147360 halves,
and each half was divided into 50 cents.
The dollar was also divided into 8507059278792630615933826294720 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 17014118555985261231867652589440 halves,
and each half was divided into 50 cents.
The dollar was also divided into 34028237111970522463735305178880 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 68056474223941044927470610357760 halves,
and each half was divided into 50 cents.
The dollar was also divided into 13611294846782088985444122075520 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 27222589693564177970888244151040 halves,
and each half was divided into 50 cents.
The dollar was also divided into 54445179387128355941776488302080 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 108890358774566711883552976604160 halves,
and each half was divided into 50 cents.
The dollar was also divided into 217780717549133423767105953208320 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 435561435098266847534211906416640 halves,
and each half was divided into 50 cents.
The dollar was also divided into 871122870196533695068423803233280 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 174224574039106739013647606666560 halves,
and each half was divided into 50 cents.
The dollar was also divided into 348449148078213478027295201333120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 696898296156426956054590402666240 halves,
and each half was divided into 50 cents.
The dollar was also divided into 139379659231245811210980804533280 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 278759318462491622421961609066560 halves,
and each half was divided into 50 cents.
The dollar was also divided into 557518636924983244843923208133120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1115037273849966489687846016266240 halves,
and each half was divided into 50 cents.
The dollar was also divided into 223007454769993297937569203253240 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 446014909539986595875138406506480 halves,
and each half was divided into 50 cents.
The dollar was also divided into 892029819079973191750276801303280 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 178405963815994638350553602606480 halves,
and each half was divided into 50 cents.
The dollar was also divided into 356811927631989276701107205212960 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 713623855263978553402214401425920 halves,
and each half was divided into 50 cents.
The dollar was also divided into 142724771052757710680442802845480 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 285449542105515421360885605690960 halves,
and each half was divided into 50 cents.
The dollar was also divided into 570898884210515442721771201381920 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 114179776842053088544354402777920 halves,
and each half was divided into 50 cents.
The dollar was also divided into 228359553684106177088708805555840 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 456719107368212354177417601111680 halves,
and each half was divided into 50 cents.
The dollar was also divided into 913438214736424708354835202223360 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 182687642947284741670967204446720 halves,
and each half was divided into 50 cents.
The dollar was also divided into 365375285894569483341934408893440 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 730750571789138966683868817786880 halves,
and each half was divided into 50 cents.
The dollar was also divided into 146150114378927793336773763557760 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 292300228757855586673547527115520 halves,
and each half was divided into 50 cents.
The dollar was also divided into 584600457515711173347095054231040 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1169200915031422346694190108462080 halves,
and each half was divided into 50 cents.
The dollar was also divided into 2338401830062844693388380216924160 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 4676803660125689386776760433848320 halves,
and each half was divided into 50 cents.
The dollar was also divided into 9353607320251378773553520867696640 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1870721464050275754710704173539320 halves,
and each half was divided into 50 cents.
The dollar was also divided into 3741442928100551509421408347078640 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 7482885856201103018842816694157280 halves,
and each half was divided into 50 cents.
The dollar was also divided into 14965771712402206037685633388314560 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 29931543424804412075371266776629120 halves,
and each half was divided into 50 cents.
The dollar was also divided into 59863086849608824150742533553258240 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 11972617369921764830148506710656480 halves,
and each half was divided into 50 cents.
The dollar was also divided into 23945234739843529660297013421312960 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 4789046947978705932059402684262560 halves,
and each half was divided into 50 cents.
The dollar was also divided into 9578093895957411864118805368525120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 1915618779191482372823761073705040 halves,
and each half was divided into 50 cents.
The dollar was also divided into 3831237558382964745647522147410080 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 7662475116765929491295044294820160 halves,
and each half was divided into 50 cents.
The dollar was also divided into 15324950233531858982590888589640320 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 30649800467063717965181777179280640 halves,
and each half was divided into 50 cents.
The dollar was also divided into 61299600934127435930363554358561280 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 12259920186825487186072710871712560 halves,
and each half was divided into 50 cents.
The dollar was also divided into 24519840373650974372145421743425120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 49039680747301948744290843486850240 halves,
and each half was divided into 50 cents.
The dollar was also divided into 98079361494603897488581686973700480 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 196158722989207794977163373947400960 halves,
and each half was divided into 50 cents.
The dollar was also divided into 392317445978415589954326746894801920 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 784634891956831179908653493789603840 halves,
and each half was divided into 50 cents.
The dollar was also divided into 156926978391366235981730698758807680 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 313853956782732471963461397517615360 halves,
and each half was divided into 50 cents.
The dollar was also divided into 62770791356546494392692279503523120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 12554158271309298878538455900704640 halves,
and each half was divided into 50 cents.
The dollar was also divided into 25108316542618597757076911801409280 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 50216633085237195514153823602818560 halves,
and each half was divided into 50 cents.
The dollar was also divided into 100433266170474391028307647205637120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 20086653234094878205661529441127440 halves,
and each half was divided into 50 cents.
The dollar was also divided into 40173306468189756411323058882254880 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 8034661293637951282264611776450960 halves,
and each half was divided into 50 cents.
The dollar was also divided into 16069322587279024564529223552919360 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 32138645174558049129058447105838720 halves,
and each half was divided into 50 cents.
The dollar was also divided into 64277290349116098258116894211675440 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 12855458069823219651623378842335080 halves,
and each half was divided into 50 cents.
The dollar was also divided into 2571091613964643930324675768467160 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 5142183227929287875649351536894320 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1028436645585857575129670307378640 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2056873291171715150259340614757280 halves,
and each half was divided into 50 cents.
The dollar was also divided into 4113746582343430300518681229514560 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 8227493164686860601037362458029120 halves,
and each half was divided into 50 cents.
The dollar was also divided into 16454986329373721202074748116058240 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 32909972658747442404149496232116480 halves,
and each half was divided into 50 cents.
The dollar was also divided into 65819945317494884808298992464232960 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 13163989063498979601658998492846920 halves,
and each half was divided into 50 cents.
The dollar was also divided into 2632797812699795920331799698569840 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 5265595625399591840663599397139680 halves,
and each half was divided into 50 cents.
The dollar was also divided into 10531191250798937681331187954279360 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 21062382501597875362662375908558720 halves,
and each half was divided into 50 cents.
The dollar was also divided into 42124765003195750725324751817117440 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 84249530006391501450649503634234880 halves,
and each half was divided into 50 cents.
The dollar was also divided into 16849866001278250290129807326867960 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 33699732002556500580259614653735920 halves,
and each half was divided into 50 cents.
The dollar was also divided into 67399464005113001160519229307471840 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 134798928002260023202384586149437680 halves,
and each half was divided into 50 cents.
The dollar was also divided into 26959785600452004640476911722987520 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 53919571200904009280953823445975040 halves,
and each half was divided into 50 cents.
The dollar was also divided into 10783914240180801856190764689194080 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 21567828480361603712381529378388160 halves,
and each half was divided into 50 cents.
The dollar was also divided into 43135656960723207424763058756776320 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 86271313921446414849526117513552640 halves,
and each half was divided into 50 cents.
The dollar was also divided into 17254262784289282969853223502705280 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 34508525568578565939706447005410560 halves,
and each half was divided into 50 cents.
The dollar was also divided into 69017051137157131879412895401021120 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 138034102274314263758825790802042240 halves,
and each half was divided into 50 cents.
The dollar was also divided into 276068204548628527517651581604084480 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 552136409097257055035303163208168960 halves,
and each half was divided into 50 cents.
The dollar was also divided into 1104272818194514110070606326416377920 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 2208545636389028220141212652832755840 halves,
and each half was divided into 50 cents.
The dollar was also divided into 4417091272778056440282425305665511680 quarters,
and each quarter was divided into 25 cents.
The dollar was also divided into 8834182545556112880564850611330233360 halves,
and each half was divided into 50 cents.
The dollar was also divided into 17668365091112245761137001222660466720 quarters,
and each quarter was divided

animals in respiratory acidosis the increased carbon dioxide and decreased plasma potassium would be expected to cause a greater decrease in the renal tubular cell pH than either alone and hence a greater reabsorption of bicarbonate.

In the present experiments, no significant extrarenal compensatory adjustments to the respiratory acidosis were detected since there were no alterations in the electrolyte patterns of plasma, muscle and bone in the nephrectomized rats exposed to carbon dioxide. In the presence of the kidneys, however, changes in the composition of muscle occurred which appear to have some importance from the standpoint of bodily compensation to respiratory acidosis.

It is interesting to relate the sodium and potassium content of rat muscle to the recent work of Levitin, Branscome and Epstein (25,28). They reported balance data on normal rats and rats maintained on low sodium and low potassium diets.¹ They measured a net negative balance of potassium (as determined by the difference between intake and urinary output) in rats eating a normal and a low sodium diet after exposure to 24 hours of 8% carbon dioxide. In rats on a low potassium diet a negative balance of sodium was observed. The decrease in muscle potassium which occurred in the rats of the present study on the normal and low sodium diets was of the same order of magnitude as the net loss of potassium from the body determined by Levitin, Branscome and Epstein, if one assumes that the muscle analyzed was repre-

¹ These animals are the same ones that are reported in this study.

sentative of the whole body muscle. The small negative balance of sodium observed by Levitin and Epstein (28) to occur when potassium depleted rats were exposed to carbon dioxide might similarly have been accounted for by losses in cell sodium, although changes in muscle sodium in the present experiments were not observed.

It was noted that the sodium and potassium of both the analyzed muscle and the calculated intracellular values always varied inversely with each other, but not to the same degree. It must be emphasized however that this was not always statistically significant.

Excluding the nephrectomized rats, the chloride content of muscle, liver and usually bone decreased in the animals in respiratory acidosis. This characteristic decrease, not statistically significant, was related to the hypochloremia of the extracellular fluid. The total tissue water remained unchanged and the calculated intracellular water did not vary significantly or in a characteristic pattern.

The decrease in muscle potassium in rats on normal and low sodium diets exposed to carbon dioxide seen in the present experiments was not observed by Cooke, Coughlin and Segar (9). Rats exposed to 10 to 15% carbon dioxide for three weeks were found by these workers to have a high normal muscle potassium and a somewhat decreased muscle sodium content which they explained on the basis of an exchange of extracellular potassium for intracellular sodium (29). Part of

the discrepancy may be due to the difference in the duration of the study. The experiments reported here were conducted for 24 hours because it was believed important to allow time for equilibrium to be established without evoking other effects such as anorexia and consequent undernutrition which might be present in more chronic experiments.

In contrast to the work of Bergstrom and Wallace (1) who found that sodium and potassium depletion of bone occurred in dogs in metabolic acidosis, there was no significant decrease in bone sodium or potassium in any of the experimental animals. In the experimental rats on a normal diet there was a significant decrease in bone phosphorus. Rats in respiratory acidosis have been observed to have increased excretion of phosphorus(25). That this phosphorous depletion did not occur in all the experiments suggests that multiple factors may be involved. It would be of interest to know whether any depletion of muscle phosphorus occurs with respiratory acidosis. Neuman and Neuman have reported that synthetic apatite equilibrated with bicarbonate exchanges phosphorus for carbon dioxide (30).

No particular effect of hypercapnia was noted on the livers of the experimental rats. In the nephrectomized rats there was a significant increase in the potassium content on exposure to respiratory acidosis, but other studies not reported here, on nephrectomized rats under slightly different conditions, failed to show this effect and it is possible

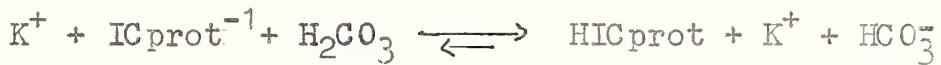
that this is not really a representative response. Cats inhaling high concentrations of carbon dioxide develop hyperkalemia and depletion of liver potassium from the stimulation of the adrenal-sympathico-hepatic system which may be in part related to glycogen depletion (31,32). This effect could not be detected below about a 10% threshold concentration of carbon dioxide. Rats in 8% carbon dioxide apparently do not have this hepatic potassium depletion.

The question must arise - does the stress of carbon dioxide inhalation with a possible concomitant release of adrenal steroids affect the electrolyte response to respiratory acidosis? Increasing secretion of 17-hydroxycorticosteroid with increasing concentrations of carbon dioxide (up to a maximal effect) occurs in dogs (33). However, a minimal concentration of carbon dioxide usually greater than 10% was required before this was noted. Aldosterone secretion has not been studied under these conditions. If a sodium sparing mechanism on the basis of increased steroid production caused increased potassium excretion in the normal experimental rats, it would seem likely that actual sodium retention would have occurred. This was not observed in the balance studies by Levitin, Branscome and Epstein (25). In potassium depleted rats, sodium excretion actually increased on exposure to carbon dioxide.

What, then, is the explanation for the fact that in respiratory acidosis only renal adjustments appear to occur while in metabolic acidosis there is an exchange of extracellular hydrogen for intracellular cations? One possibility

is that experimental metabolic acidosis is generally produced by the addition of strong mineral acids with nondiffusible anions to the extracellular fluid. The immediate effect produces an extracellular acidosis. Hydrogen ions tend to move intracellularly in exchange for intracellular cations which enter the extracellular fluid in order to maintain ionic equilibrium. Carbon dioxide, on the other hand, is believed to be almost immediately permeable to the cell membrane (34). Thus in respiratory acidosis one would expect an increase in pCO_2 both intra and extracellularly without a disproportionate pH shift between the two phases. In the absence of renal function there might be little impetus for adjustments to occur.

Strong mineral acids (hydrochloric) can be buffered by salts of weak acids (sodium bicarbonate, sodium or potassium proteinate). Carbonic acid, on the other hand, cannot be buffered by sodium bicarbonate although it is a stronger acid than most proteins. The reaction



(which results in a loss of cellular potassium ion) probably occurs to a minimal extent in nephrectomized rats exposed to carbon dioxide, but is prevented from proceeding because of the accumulation of potassium ions in the extracellular fluid. However, when the kidneys are intact, potassium, which is lost from muscle because of the buffering function of intracellular protein, is removed in the urine

¹ Intracellular proteinate:

and further hydrogen ion accumulation and potassium loss by muscle is allowed to continue.

These observations underline the importance of the kidneys in defense against respiratory acidosis. Not only do they excrete some of the added load of hydrogen ion as ammonium and titratable acid, and reabsorb bicarbonate to restore plasma pH toward normal, but they permit cellular buffering of hydrogen ion to take place by excreting intracellular cation (potassium) before it accumulates. The burden thrown on the kidneys is seen to be all the greater when it is realized that, unlike metabolic acidosis, bone sodium does not exchange appreciably with hydrogen when animals are exposed to carbon dioxide.

TABLE I
Electrolyte Composition of Diet

	Na mEq./gm.	K mEq./gm.	Cl mEq./gm.
Normal Diet	0.115	0.128	0.135
Low Sodium Diet	0.0057	0.160	0.138
Low Potassium Diet	0.167	0.143	0.00727

TABLE II
Comparison of Thigh and Abdominal Muscle

	%H ₂ O	%Fat	Cl ¹	Na ¹	K ¹	Na ² _i	K ² _i
Room Air (4) ³							
Thigh	75.1 ⁴ 0.6 ⁴	3.0 0.8	5.7 0.3	8.2 0.4	46.4 1.5	3.1 1.4	156.0 4.7
Abd.	74.6 0.7	4.4 0.7	8.4 0.8	11.7 1.0	42.5 1.0	3.1 0.3	147.9 4.1
p ⁵			****	****	**	ns	*
Carbon Dioxide (4)							
Thigh	75.1 1.2	2.7 1.1	4.9 0.6	9.7 1.3	43.7 0.6	9.8 2.1	148.2 3.7
Abd.	75.6 0.6	2.8 0.3	7.6 1.1	12.9 1.3	41.2 0.8	8.6 2.6	145.7 2.1
p			***	**	***	ns	ns

¹ MEq. per 100 gm. FFDM.

² MEq. per kg. intracellular water.

³ Number of rats.

⁴ Mean \pm standard deviation.

⁵ Probability using Student's T test for significance.

* < .05, ** < .01, *** < .005, **** < .001, ns - not significant.

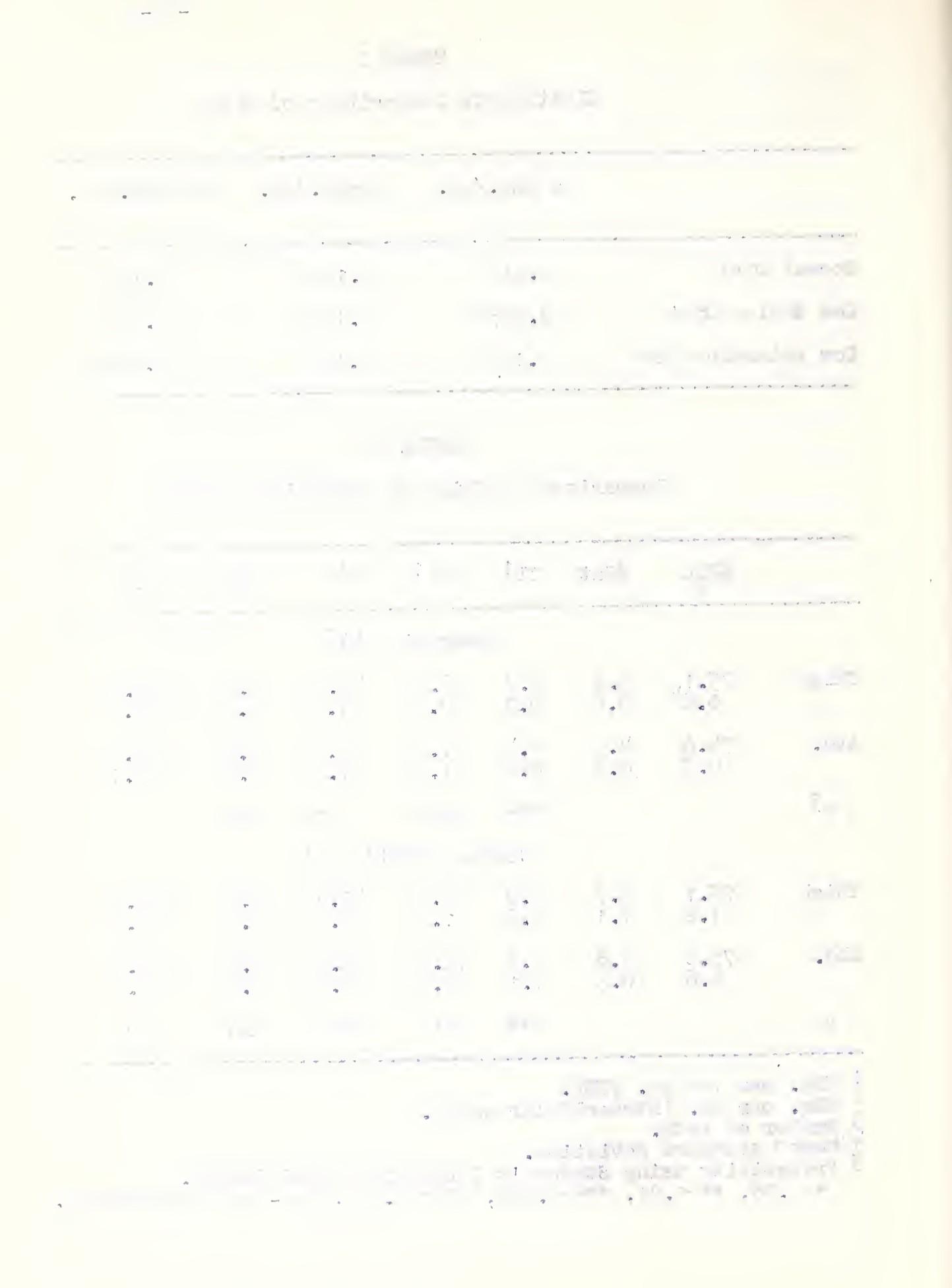


TABLE III

Exsanguination of Experimental Rats in Room Air and Carbon Dioxide

	Room Air ¹	CO ₂ Hood ²	p ³
Muscle			
% H ₂ O/sample	76.0 0.84	75.6 0.7	ns
% Fat/sample	1.00 0.64	1.62 0.75	ns
Fat Free Dry Muscle			
Na mEq./100 gm.	9.2 0.9	7.8 1.0	**
K mEq./100 gm.	45.8 1.4	46.1 0.5	ns
Cl mEq./100 gm.	4.2 0.8	4.8 0.2	ns
Intracellular H₂O			
Na _i mEq./kg.	11.7 5.2	4.7 3.4	*
K _i mEq./kg.	155.3 7.8	158.7 2.5	ns
Plasma			
CO ₂ mEq./L.	30.7 3.8	34.8 1.6	*
Na mEq./L.	150.6 4.6	151.2 3.8	ns
K mEq./L.	4.02 0.43	4.46 0.56	ns
Cl mEq./L.	99.2 1.9	100.1 2.3	ns

¹ 10 female rats weighing 180-227 gm. at sacrifice.² 8 male rats weighing 282-502 gm. at sacrifice.³ Probability using Student's T test for significance.

* <.025, ** <.01, ns - not significant.

⁴ Mean \pm standard deviation.

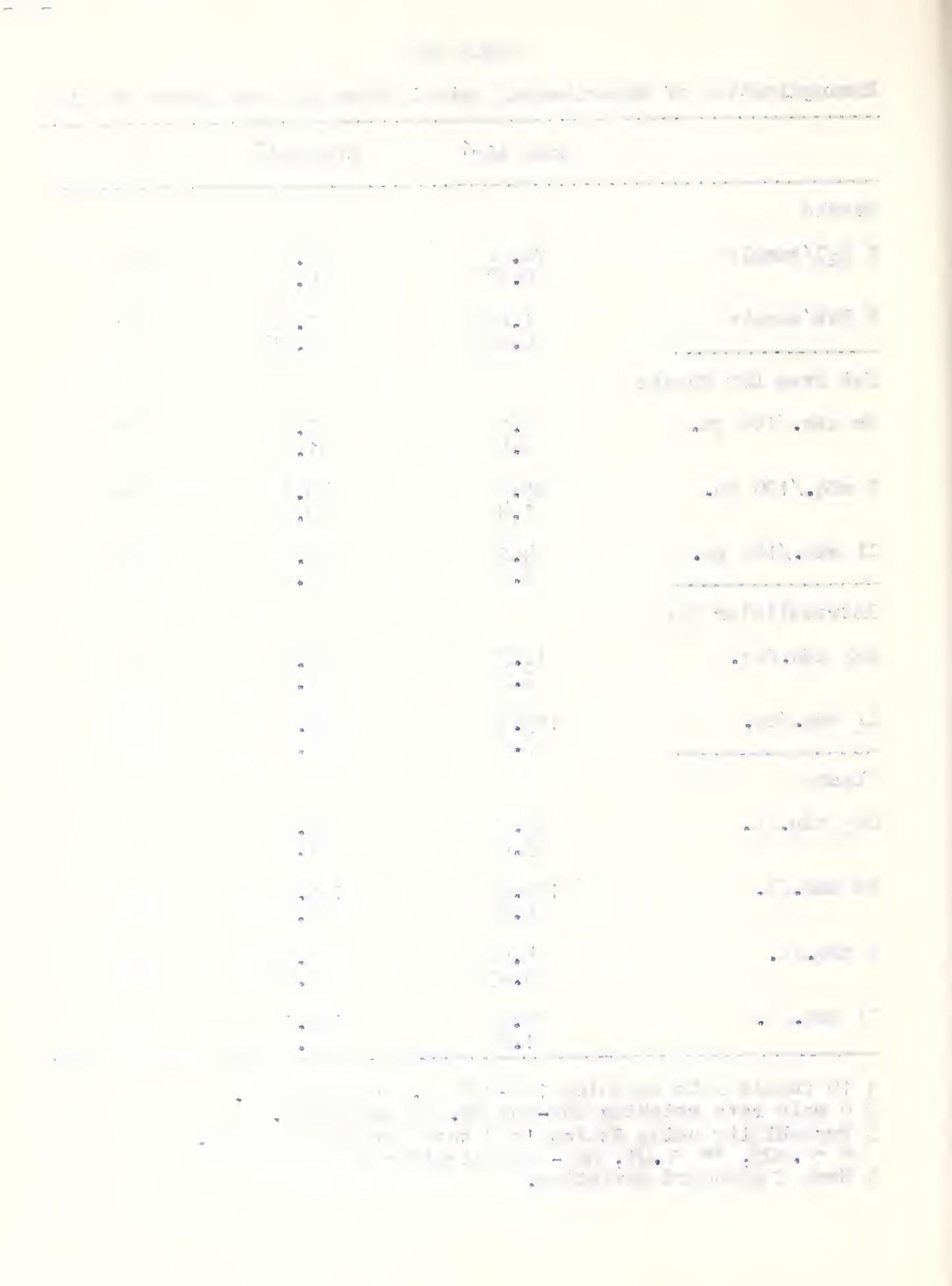


TABLE IV
The Effect of Respiratory Acidosis on Plasma

	CO_2 mEq./L.	Cl mEq./L.	Na mEq./L.	K mEq./L.
Normal Diet Group I				
Room Air (10) ¹	24.4 2.7 ²	105.6 1.3	148.6 2.2	3.48 0.24
CO_2 (10)	30.7 3.8	99.2 1.9	150.6 4.6	4.02 0.43
p ³	**	***	ns	**
Nephrectomy Group II				
Room Air (7)	21.0 2.0	93.3 ⁴ 2.4	148.8 4.5	7.09 1.08
CO_2 (6)	21.1 1.6	94.3 ⁴ 2.4	151.4 5.2	7.82 0.31
p	ns	ns	ns	ns
Low Sodium Diet Group III				
Room Air (4)	25.9 0.5	106.7 1.4	151.1 0.6	3.95 0.59
CO_2 (4)	32.3 1.3	97.9 1.7	152.0 6.3	4.10 0.2
p	***	***	ns	ns
Low Potassium Diet Group IV				
Room Air (6)	29.6 1.8	99.5 2.1	146.9 1.8	2.00 0.20
CO_2 (4)	38.9 0.3	93.0 1.7	150.3 4.4	2.62 0.12
p	***	***	ns	*

¹ Number of rats.

² Mean \pm standard deviation.

³ Probability using Student's T test for significance.

* <.025, ** <.005, *** <.001, ns - not significant.

⁴ Determined by the Volhard titration. This method averages about 6 mEq./L. less than the chloride concentration determined by potentiometric titration.

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TABLE V
The Effect of Respiratory Acidosis on Muscle

	Normal Diet Room Air (10) ¹	Group I CO ₂ (10)	p ²	Nephrectomy Room Air (7)	Group II CO ₂ (6)	p
% H ₂ O/sample	76.8 0.63	76.0 0.8	ns	77.0 1.4	76.4 1.0	ns
% Fat/sample	0.73 0.34	1.00 0.64	ns	1.46 0.91	1.50 0.74	ns
Fat-Free Dry Muscle						
Na mEq./100 gm.	9.0 0.9	9.2 0.9	ns	7.7 0.4	7.5 0.6	ns
K mEq./100 gm.	47.3 1.2	45.8 1.4	*	48.7 0.8	48.7 0.8	ns
Cl mEq./100 gm.	4.9 0.8	4.2 0.8	ns	5.2 0.4	5.2 0.7	ns
Fat-Free Wet Muscle						
H ₂ O ⁴ /kg. ³	680.6 16.4	681.8 17.3	ns	676.1 14.7	667.7 19.8	ns
Na mEq./kg.	20.4 2.5	21.3 2.2	ns	16.9 1.2	16.8 1.9	ns
K mEq./kg.	107.2 3.0	106.1 3.0	ns	106.5 3.2	109.2 2.9	ns
Intracellular H ₂ O						
Na _i mEq./kg.	9.3 5.0	11.7 5.2	ns	1.1 0.8	0.6 0.9	ns
K _i mEq./kg.	157.2 6.6	155.3 7.8	ns	156.2 7.4	162.5 7.9	ns

¹ Number of rats.

² Probability using Student's T test for significance.

* < .025, ns - not significant.

³ Mean \pm standard deviation.

⁴ Gm. intracellular water.

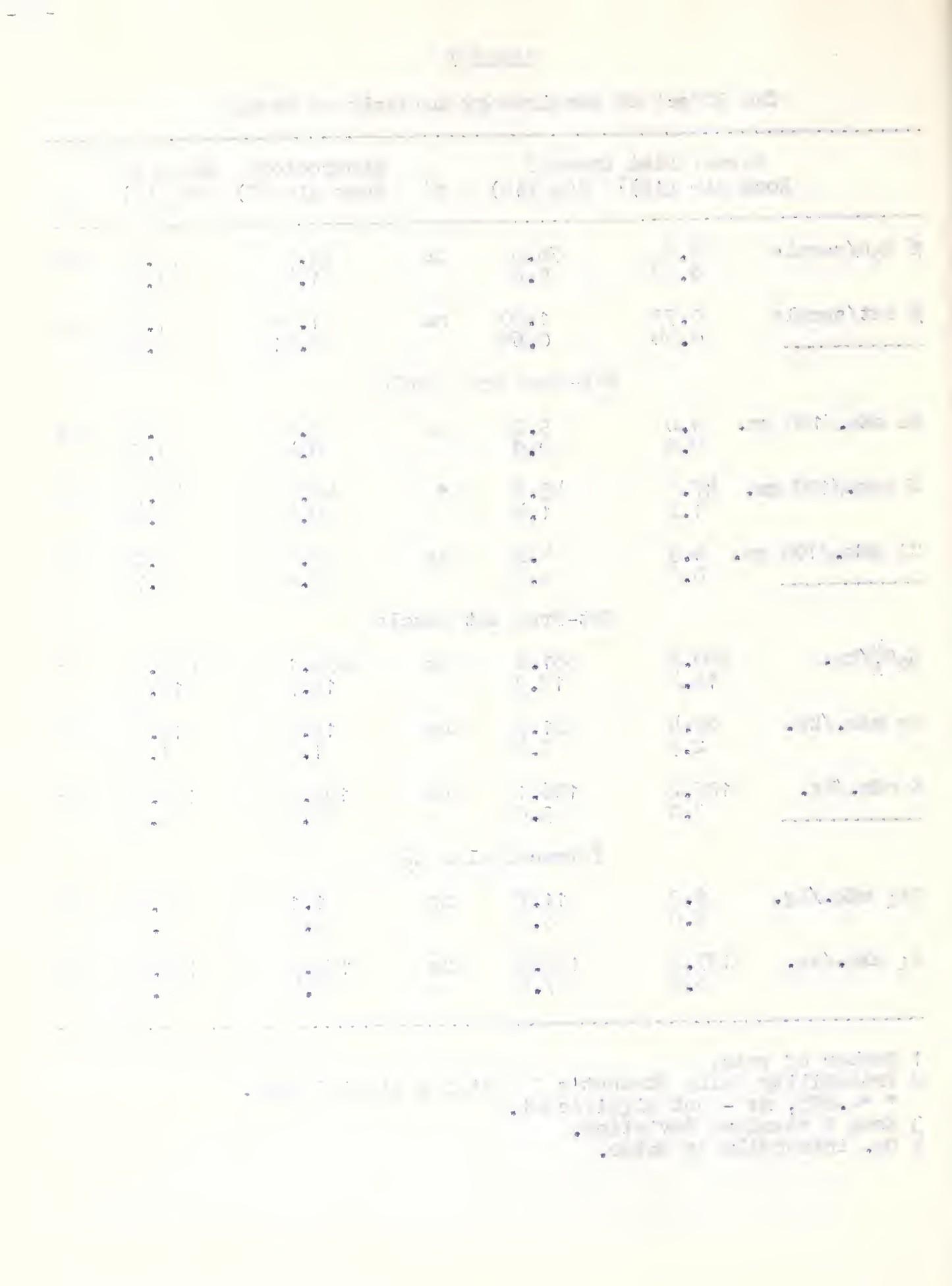


TABLE VI
The Effect of Respiratory Acidosis on Muscle

	Low Sodium Diet Room Air (4) ¹	Group III CO ₂ (4)	p ²	Low Potassium Diet Room Air (6)	Group IV CO ₂ (4)	p
% H ₂ O/sample	75.1 0.63	75.1 1.2	ns	74.1 0.3	73.9 0.5	ns
% Fat/sample	3.02 0.76	2.67 1.08	ns	3.75 1.28	3.61 0.61	ns
Fat-Free Dry Muscle						
Na mEq./100 gm.	8.2 0.4	9.7 1.3	ns	13.3 1.5	12.3 0.3	ns
K mEq./100 gm.	46.4 1.5	43.7 0.5	**	37.7 2.2	39.2 0.8	ns
Cl mEq./100 gm.	5.7 0.3	4.9 0.6	ns	4.9 0.5	4.6 0.3	ns
Fat-Free Wet Muscle						
H ₂ O _i ⁴ /kg.	669.2 3.4	671.1 4.5	ns	671.6 9.3	665.6 2.4	ns
Na mEq./kg.	18.6 0.7	22.2 2.5	*	30.6 3.5	28.7 0.5	ns
K mEq./kg.	104.8 3.4	99.8 2.8	ns	86.6 4.8	91.4 1.9	ns
Intracellular H ₂ O						
Na _i mEq./kg.	3.1 1.4	9.8 2.1	***	23.6 3.8	19.8 0.8	ns
K _i mEq./kg.	156.0 4.7	148.2 3.7	*	128.6 6.1	137.0 2.5	*

¹ Number of rats.

² Probability using Student's T test for significance.

* <.05, ** <.025, *** <.005, ns - not significant.

³ Mean \pm standard deviation.

⁴ Gm. intracellular water.

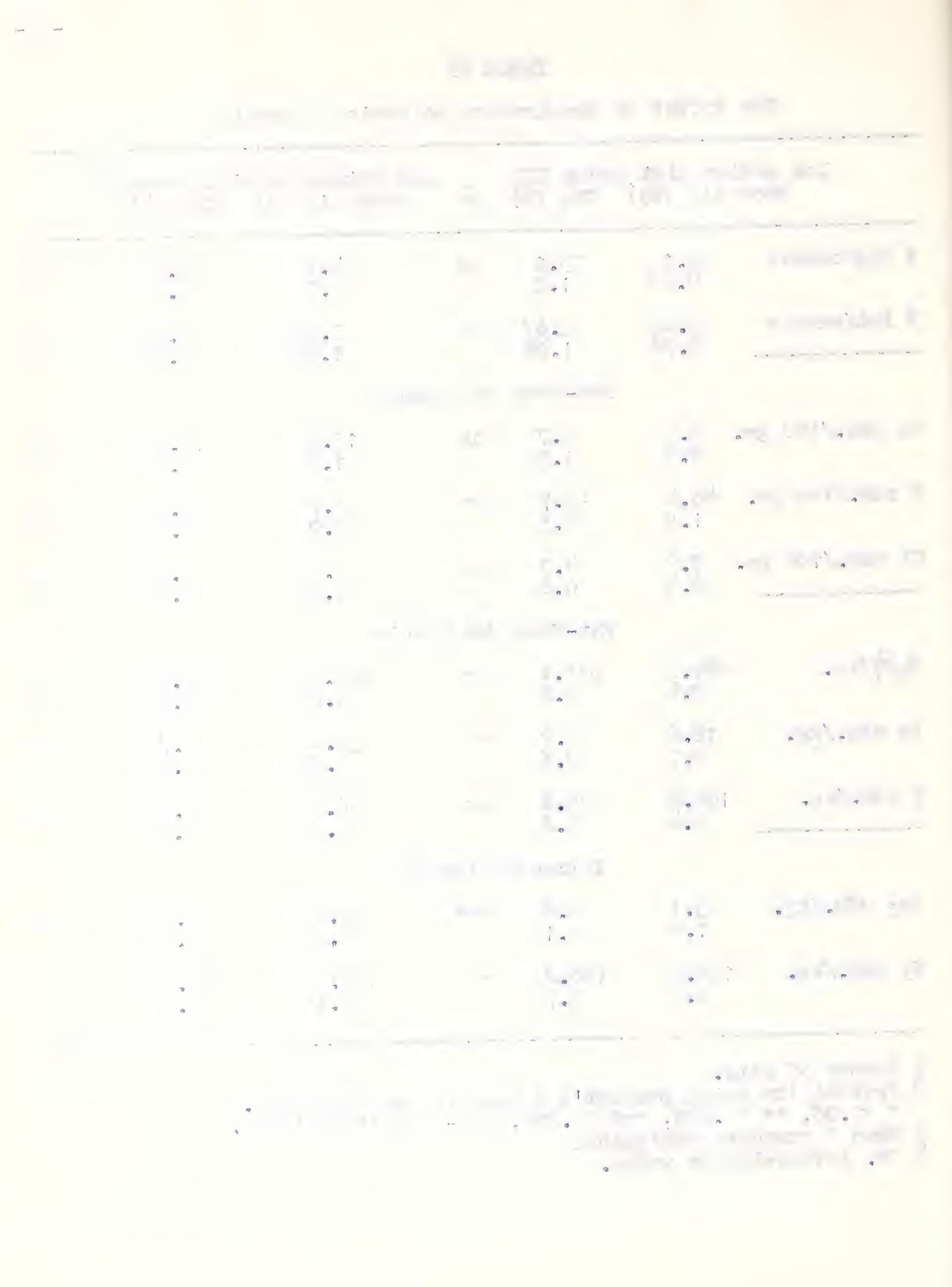


TABLE VII
The Effect of Respiratory Acidosis on Liver

	% H ₂ O	% Fat	Na ¹	K ¹	Cl ¹
Normal Diet Group I					
Room Air (10) ²	73.5 1.13	1.22 0.33	10.7 0.9	36.6 1.2	10.5 0.9
CO ₂ (10)	73.0 0.6	1.28 0.43	10.9 0.7	36.1 1.5	9.8 1.5
p ⁴	ns	ns	ns	ns	ns
Nephrectomy Group II					
Room Air (7)	73.0 0.6	1.22 0.33	11.0 1.1	35.4 1.1	9.2 1.0
CO ₂ (6)	73.5 1.1	1.28 0.43	11.6 2.1	36.9 1.1	9.0 1.6
p	ns	ns	ns	*	ns
Low Sodium Diet Group III					
Room Air (4)	70.6 0.2	4.09 0.95	9.3 0.2	35.5 0.7	11.6 0.3
CO ₂ (4)	71.7 0.3	1.85 0.26	9.6 0.8	35.3 1.8	9.9 0.6
p	***	**	ns	ns	**

¹ MEq./100gm. fat free dry liver.

² Number of rats.

³ Mean \pm standard deviation.

⁴ Probability using Student's T test for significance.

* <.05, ** <.005, *** < .001, ns - not significant.

TABLE VIII
The Effect of Respiratory Acidosis on Bone

	% H ₂ O	Na ¹	K ¹	Cl ¹	P ²
Normal Diet Group I					
Room Air (10) ³	18.7 ₄ 1.0	28.3 0.4	1.9 0.3	1.7 0.6	130.4 2.2
CO ₂ (10)	20.8 2.6	28.0 0.7	2.5 0.6	1.9 0.4	126.9 3.1
p ⁵	ns	ns	*	ns	**
Nephrectomy Group II					
Room Air (7)	28.8 4.4	27.7 1.1	4.5 0.8	2.6 0.8	124.3 4.4
CO ₂ (6)	27.8 4.8	27.3 0.6	4.4 1.1	2.7 0.6	125.7 4.9
p	ns	ns	ns	ns	ns
Low Sodium Diet Group II					
Room Air (4)	27.8 3.7	27.5 0.4	4.2 0.8	3.2 0.4	127.0 4.1
CO ₂ (4)	24.9 2.0	28.4 1.1	3.4 0.6	2.3 0.4	130.0 5.2
p	ns	ns	ns	*	ns
Low Potassium Diet Group III					
Room Air (6)	24.5 2.1	26.3 0.2	3.4 0.5	3.0 0.3	126.1 0.3
CO ₂ (4)	21.3 2.1	26.8 0.3	3.0 0.4	2.2 0.1	126.7 1.5
p	ns	ns	ns	***	ns

¹ MEq./100 gm. dry bone.² Mgm./gm. dry bone.³ Number of rats.⁴ Mean \pm standard deviation.⁵ Probability using Student's T test for significance.
* < .025, ** < .01, *** < .005, ns - not significant.

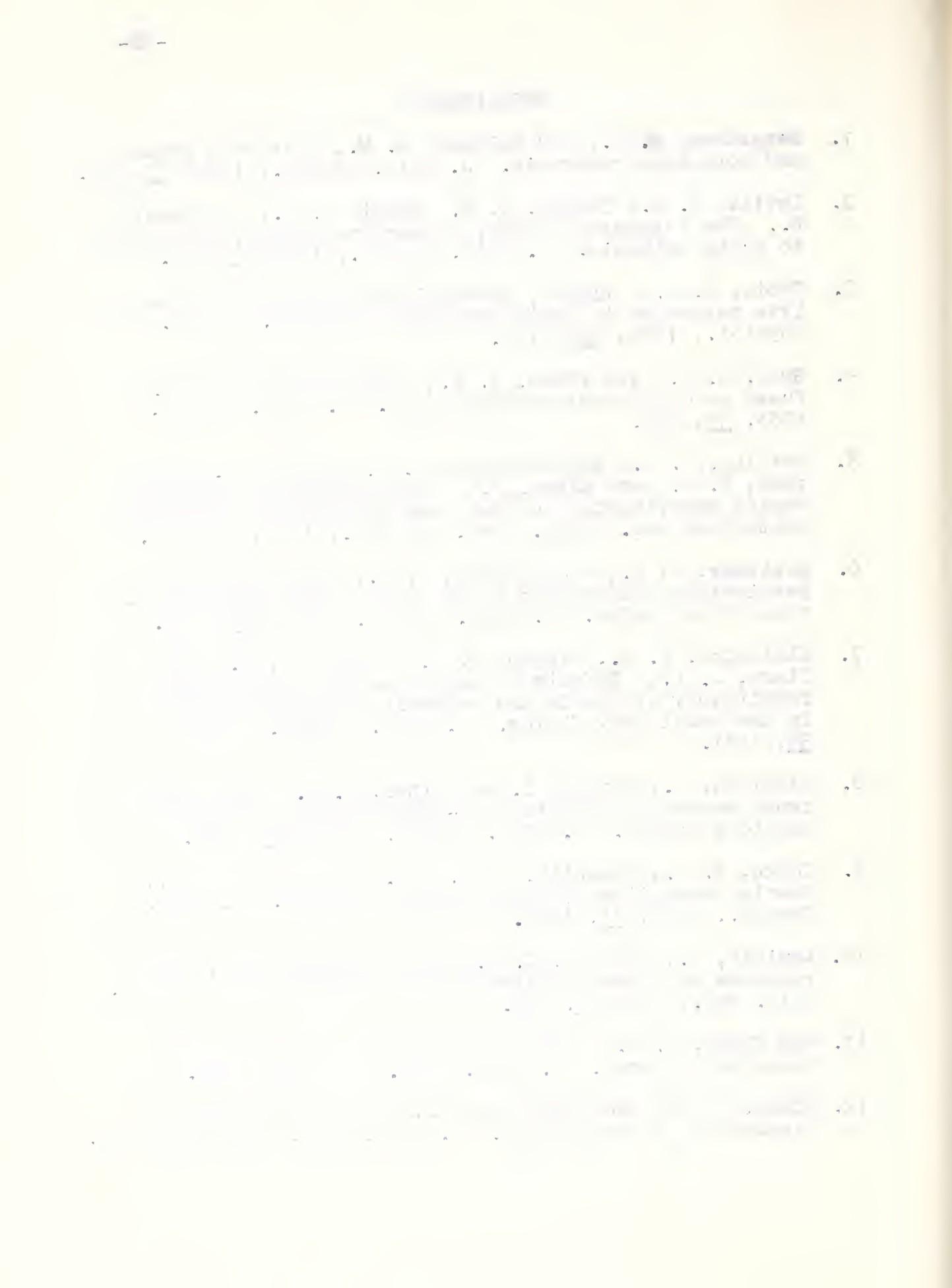
SUMMARY

1. The effect of respiratory acidosis induced in rats by 24 hours exposure to 8% carbon dioxide on
 - a. Plasma 1) Normal rats and those maintained on low sodium and low potassium diets had an increase of carbon dioxide content and a decrease in chloride concentration of about 6 mEq. per liter respectively.
2) Normal rats and those on a low potassium diet had a slight increase in potassium concentration.
 - b. Muscle Normal rats and those on a low sodium diet had a decrease of 1.5 and 2.7 mEq. potassium per 100 gm. fat-free dry muscle respectively.
 - c. Liver No significant change in the sodium or potassium concentration was noted in the rats on normal, low sodium or low potassium diets.
 - d. Bone 1) There was a slight increase in the potassium concentration of dry bone in the normal rats.
2) There was a decrease of 3.5 mg. phosphorus per gm. dry bone in normal rats.
2. There were no significant changes in plasma, muscle, or bone electrolytes in nephrectomized rats in respiratory acidosis.

3. There were significant differences in the chloride, potassium and sodium concentrations of fat-free dry muscle from the abdomen and thigh of rats.

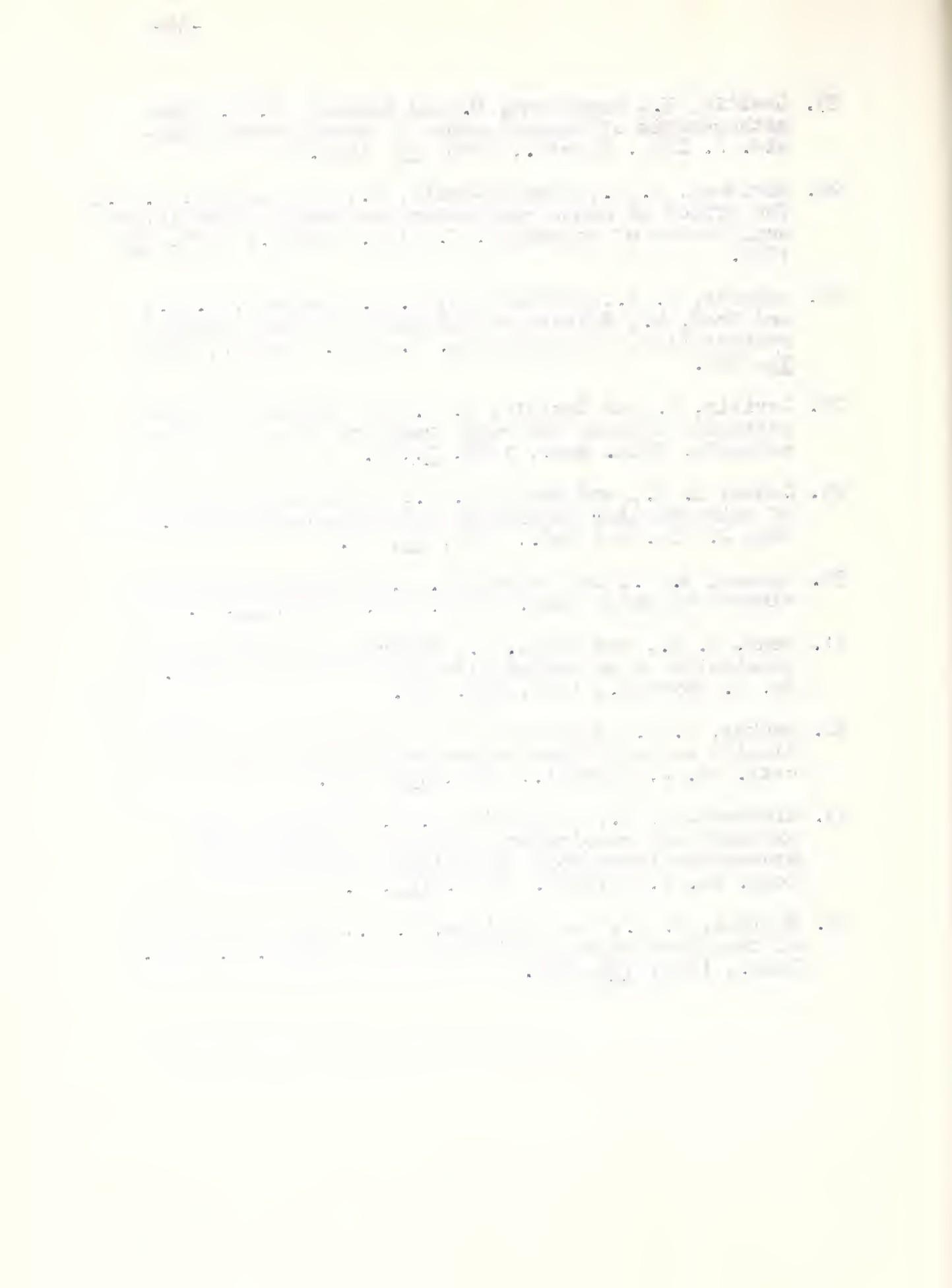
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